REMARKS

Claims 1-8, 11-13, and 15-20 were pending. Applicants have herein amended claims 1, 11, and 15, and cancelled claim 20. Support for the amendments to the claims can be found throughout the specification, *e.g.*, at paragraph [0137] of the US publication of the present application, US 2006/0058522. No new matter has been added. Accordingly, claims 1-8, 11-13, and 15-19 are pending.

In light of the amendments and the remarks herein, Applicants respectfully request reconsideration and allowance of the pending claims.

Lack of Unity

Applicants have herein amended claim 1 to remove non-elected Groups II-LVI from its scope, *i.e.*, claim 1 has been amended to remove the embodiments where CR^3R^4 form a ring and where R^5 can contain a Het ring; in addition, claim 1 recites that A is phenyl. Accordingly, Applicants respectfully assert that the presently pending claims are directed to Group I and request withdrawal of the Lack of Unity rejection.

Rejections under 35 U.S.C. § 112, first paragraph

The Examiner rejected claims 11, 15, and 25 as not fully enabled. In particular, the Examiner asserted that the specification, while being enabling for treating certain diseases that benefit from the inhibition of IKK-2, does not reasonably provide enablement for treating all of the diseases/disorders encompassed by such inhibition. In addition, the Examiner stated that cancer has "no known cure," and that "blanket" prevention or treatment of cancer was not demonstrated in the art. Applicants respectfully disagree.

Claim 11 has been amended to recite a particular list of inflammatory diseases; this list is narrower than the claim as unamended and finds support in paragraph [0137] of the US publication of the above-referenced application. Claim 15 has also been amended to recite a method of treating or reducing the risk of cancer. Applicants respectfully assert that the claims as amended are fully enabled by the present specification. As set forth in the present

specification in paragraphs [0005]-[0011], [0135]-[0142], IKK-2 is involved in the regulation of NF-kB, which has been reported to play a significant role in the development of cancer and metastasis. The specification demonstrates that the compounds of the present invention inhibit IKK-2 at low IC_{50} (nanomolar) values; *see* para. [0360] of the US Publication 2006/0058522. In addition, IKK/NF-kB signaling is acknowledged in the art to play a pivotal role in the coordination of inflammatory responses and in the development of cancer and metastasis; indeed, NF-kB is an art-acknowledged target for the treatment of inflammatory diseases and cancers; *see* Luo *et al.*, "IKK/NF-kB signaling: balancing life and death – a new approach to cancer therapy," J. of Clin. Investigation, Vol. 115(10):2625-2632 (October 2005); Orlowski *et al.*, "NF-kB as a therapeutic target in cancer," TRENDS in Molecular Medicine, Vol. 8(8):385-389 (August 2002); and Karin *et al.*, "NF-kB in cancer: from innocent bystander to major culprit," Nat. Rev. Cancer, Vol. 2:301-310 (2002), copies of which are attached hereto and submitted in a Supplemental IDS. In the Examiner's own words, "NF-kB is known to be implicated in diseases/disorders such as inflammation, allergy, rheumatoid arthritis, GVHD, rhinitis, asthma and in certain proliferative diseases such as cancer;" *see* Office Action at page 4. Accordingly, Applicants respectfully assert that the present claims are in fact enabled, as the correlation between IKK/NF-kB signaling and a variety of inflammatory diseases and cancers is accepted in the art, and the inhibition of IKK-2 by the present compounds has been demonstrated.

With respect to claim 15, presently directed to methods for treating or reducing the risk of cancer, Applicants respectfully note that the claim does not recite a "blanket" cure or prevention of cancer, as suggested by the Examiner. While there may be no universal "cure" for cancer, there are certainly many compounds that can alleviate the symptoms associated with cancer or reduce the risk of cancer, including metastatic cancer. Accordingly, Applicants respectfully assert that the Examiner's standard for enablement in the present case is incorrect. The present claims are enabled for the treatment (*e.g.* therapeutic effect) or reduction of risk of cancer, as inhibition of NF-kB signaling is reasonably correlated with a beneficial treatment or reduction in the risk of cancer, particularly metastatic cancer, as set forth in the present application at

paragraph [0011] and in the attached references. The demonstrated activity of the compounds of the present claims in inhibiting IKK-2 activity, a kinase which is known to be active in the NF-kB signaling pathway, would reasonably be expected by those having ordinary skill in the art to be beneficial in the treatment or prevention of cancer. Accordingly, Applicants respectfully assert that the present claims are in fact enabled by the specification as filed, and request withdrawal of the rejections.

Double Patenting

The Examiner provisionally rejected claims 1-8, 11-13, and 15-20 on the ground of nonstatutory double patenting over claims 1-11, 21, 26 and 33 of co-pending Application No. 09/868,884. The Examiner stated that the substitutent $CR^3R^4X\text{-}R^5$ in the present application corresponds to CH_2R^{11}, where R^{11} is a group $NR^{21}R^{22}$, of the co-pending application.

Applicants respectfully disagree. Applicants first respectfully note that the corresponding group of the co-pending application is actually $(CH_2)_nR^{11}$, where n is 2, 3, or 4. Importantly, n cannot be 1, eliminating the Examiner's alleged overlap in claim scope between the present and co-pending case. Moreover, the Table in the present specification at paragraph [0360] compares certain of the presently claimed compounds to certain of the compounds in the cited co-pending case. The compounds listed from the co-pending case have a chain including an oxygen and two carbon atoms ($-O\text{-}CH_2\text{-}CH_2-$) between the phenyl carbon atom and the N atom of the substituent, while the present compounds have only a single carbon atom linker ($-CH_2-$) between the phenyl carbon atom and the N atom of the substituent; this possibility of only a $-CH_2-$ linker is not envisaged or possible in the co-pending case. As can be seen in the Table, the compounds of the present application demonstrate a significantly enhanced activity in inhibiting IKK-2, which Applicants believe to be a function of the different (shorter) spacing between the N group and the phenyl carbon atom as compared to the co-pending case. In view of the above, Applicants respectfully request that the double patenting rejection be withdrawn, as the presently claimed compounds are both novel and non-obvious over the co-pending application.

CONCLUSION

Applicants respectfully assert that all claims are in condition for allowance, which action is hereby requested. The Examiner is invited to telephone the under-signed attorney if such would expedite prosecution.

Please charge Deposit Account No. 06-1050 for the Petition for Extension of Time fee (3 months). Please apply any other charges or credits to deposit account 06-1050.

Respectfully submitted,

Date: 2/11/08

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